08/794,851

```
Trying 11180...Open

PLEASE ENTER HOST PORT ID:
PLEASE ENTER HOST PORT ID:x
LOGINID:d180JXR
PASSWORD:
TERMINAL (ENTER 1, 2, 3, 4, OR ?):□3


  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *                                                               *
  *           Welcome to MESSENGER (APS Text) at USPTO            *
  *                                                               *
  *                                                               *
  *    The USPTO production files are current through:            *
  *    June 1,1999  for U.S. Patent Text Data.                    *
  *    June 1,1999  for U.S. Current Classification Data.         *
  *    June 1,1999  for U.S. Patent Image Data.                   *
  *                                                               *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *       * PLEASE USE 305-9000 FOR NEW TELEPHONE NUMBER *        *
  *                                                               *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  * More U.S. patent data is now available on APS.  The new      *
  * USOCR file contains patents issued in 1970, plus some        *
  * patents that were missing from the USPAT file.  See the      *
  * Patents News Folder under the Public Folders in e-mail for   *
  * more information on using the new file.  Thank you.          *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *  DISCLAIMER:                                                  *
  *  Neither the United States Government, nor any agency         *
  *  thereof, nor any of their contractors, subcontractors or     *
  *  employees make any warranty, expressed or implied,           *
  *  including any warranty of marketability of fitness for a     *
  *  particular purpose; nor assumes any legal liability or       *
  *  responsibility for any party's use, or the results of        *
  *  such, of the data.                                           *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *                Help Desk --> 703-305-9000                     *
  *                                                               *
  *    The Help Desk is staffed for APS support 7 days/week.      *
  *      Monday through Friday:       6:30am - 9:00pm            *
  *      Saturday, Sunday, Holidays: 8:30am - 5:00 pm            *
  *                                                               *
  *    The Help Desk staff at this number will handle all APS     *
  *    related questions.                                         *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *    >>>>>>>>>>>>> NEW SUNDAY HOURS !!! <<<<<<<<<<<<<           *
  *                                                               *
  *    The APS is available:                                      *
  *            6:30am - 9:00pm Monday through Friday              *
  *            7:30am - 5:00pm Saturday, Sunday, Holidays         *
  *                                                               *
  *      APS is unavailable Thanksgiving Day, Christmas Day,      *
  *      and New Year's Day.                                      *
  *                                                               *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
FILE 'USPAT' ENTERED AT 12:34:33 ON 06 JUN 1999

  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *        U. S.   P A T E N T   T E X T   F I L E                *
  *                                                               *
  *  THE WEEKLY PATENT TEXT AND IMAGE DATA IS CURRENT             *
  *  THROUGH June 1,1999.                                         *
  *                                                               *
  *                                                               *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> s (435/89 or 435/91 or 435/91.2 or 435/91.52)/ccls

          102 435/89/CCLS
            0 435/91/CCLS
         1367 435/91.2/CCLS
           83 435/91.52/CCLS
L1       1510 (435/89 OR 435/91 OR 435/91.2 OR 435/91.52)/CCLS
```

```
=> s (435/89 or  435/91 or 435/91.2 or 435/91.52)/cor

            43 435/89/COR
             0 435/91/COR
           192 435/91.2/COR
            12 435/91.52/COR
L2         247 (435/89 OR  435/91 OR 435/91.2 OR 435/91.52)/COR

=> s l2 and ligase  and array

          6448 LIGASE
        187983 ARRAY
L3          13 L2 AND LIGASE  AND ARRAY

=> d 1-13
```

1. 5,882,904, Mar. 16, 1999, Thermococcus barossii DNA polymerase mutants; William A. Riedl, et al., **435/91.2**, 194 [IMAGE AVAILABLE]

2. 5,858,732, Jan. 12, 1999, Wide dynamic range nucleic acid detection using an aggregate primer series; Natalie A. Solomon, et al., **435/91.2**, 5, 6, 91.1; 536/24.3, 24.31, 24.33 [IMAGE AVAILABLE]

3. 5,854,033, Dec. 29, 1998, Rolling circle replication reporter systems; Paul M. Lizardi, **435/91.2**, 6, 91.1; 536/23.1, 24.3 [IMAGE AVAILABLE]

4. 5,849,544, Dec. 15, 1998, Amplification and detection process; Raymond John Harris, et al., **435/91.2**, 6 [IMAGE AVAILABLE]

5. 5,705,366, Jan. 6, 1998, Coamplification of target nucleic acids using volume exclusion agent in reaction composition, test kit and test device useful therefor; John W. Backus, **435/91.2**, 5, 6; 536/23.1, 24.3, 24.32, 24.33 [IMAGE AVAILABLE]

6. 5,654,179, Aug. 5, 1997, Nucleic acid preparation methods; Lily Lin, **435/91.2**, 270; 436/177, 825; 536/25.4, 25.41, 25.42 [IMAGE AVAILABLE]

7. 5,614,388, Mar. 25, 1997, PCR primers for detection of legionella species and methods for controlling visual intensity in hybridization assays; Teresa K.H. Picone, et al., **435/91.2**, 6, 91.1, 822; 436/94; 536/23.1, 23.7, 24.32, 24.33, 25.3 [IMAGE AVAILABLE]

8. 5,612,201, Mar. 18, 1997, Isolated nucleic acid molecules useful in determining expression of a tumor rejection antigen precursor; Etienne De Plaen, et al., **435/91.2**, 6; 536/23.1, 24.33 [IMAGE AVAILABLE]

9. 5,565,339, Oct. 15, 1996, Compositions and methods for inhibiting dimerization of primers during storage of polymerase chain reaction reagents; Will Bloch, et al., **435/91.2**; 422/102; 435/6 [IMAGE AVAILABLE]

10. 5,559,013, Sep. 24, 1996, Method of amplification using intermediate renaturation step; John W. Backus, et al., **435/91.2**, 5, 6; 536/24.3, 24.33 [IMAGE AVAILABLE]

11. 5,427,932, Jun. 27, 1995, Repeat sequence chromosome specific nucleic acid probes and methods of preparing and using; Heinz-Ulrich G. Weier, et al., **435/91.2**, 6, 810; 436/501; 536/22.1, 23.1, 24.3, 24.31, 24.33 [IMAGE AVAILABLE]

12. 5,278,051, Jan. 11, 1994, Construction of geometrical objects from polynucleotides; Nadrian C. Seeman, et al., **435/91.52**, 91.3, 91.51; 536/23.1, 24.2 [IMAGE AVAILABLE]

13. 4,888,286, Dec. 19, 1989, Production of gene and protein analogs through synthetic gene design using double stranded synthetic oligonucleotides; Roberto Crea, **435/91.52**, 69.4, 91.53; 536/23.51 [IMAGE AVAILABLE]

```
=> d 1-13 cit date kwic
```

1. 5,882,904, Mar. 16, 1999, Thermococcus barossii DNA polymerase mutants; William A. Riedl, et al., **435/91.2**, 194 [IMAGE AVAILABLE]

Document Number 2

Entry 2 of 7 File: USPT Nov 3, 1998

US-PAT-NO: 5830711
DOCUMENT-IDENTIFIER: US 5830711 A

TITLE: Thermostable ligase mediated DNA amplification system for the detection of genetic diseases
DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Barany; Francis	New York	NY	N/A	N/A
Zebala; John	New York	NY	N/A	N/A
Nickerson; Deborah	Seattle	WA	N/A	N/A
Kaiser, Jr.; Robert J.	Seatlle	WA	N/A	N/A
Hood; Leroy	Seatlle	WA	N/A	N/A

ASSIGNEE INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Cornell Research Foundation, Inc.	Ithaca	NY	N/A	N/A	02
California Institute of Technology	Pasadena	CA	N/A	N/A	02

APPL-NO: 8/ 462221
DATE FILED: June 5, 1995
PARENT-CASE:
This is a continuation of application Ser. No. 08/343,785 filed on Nov. 22, 1994, now U.S. Pat. No. 5,494,810 which is a continuation of application Ser. No. 07/971,095 filed on Nov. 2, 1992, now abandoned, which is a continuation in part of application Ser. No. 07/518,447 filed on May 3, 1990, now abandoned.

INT-CL: [6] C12 P 19/34, C12 Q 2/68, C07 H 21/00, C07 H 21/04
US-CL-ISSUED: 435/91.1; 435/6, 435/91.2, 536/22.1, 536/23.1, 536/24.3, 536/25.32, 536/25.4
US-CL-CURRENT: 435/91.1; 435/6, 435/91.2, 536/22.1, 536/23.1, 536/24.3, 536/25.32, 536/25.4
FIELD-OF-SEARCH: 435/6, 435/91.1, 435/91.2, 536/22.1, 536/23.1, 536/24.3, 536/25.32, 536/25.4

REF-CITED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
4683202	July 1987	Mullis	435/91
4749647	June 1988	Thomas et al.	435/6
4889818	December 1989	Gelfand et al.	435/194
4988617	January 1991	Landegren et al.	435/6
5242794	September 1993	Whiteley et al.	435/6
5494810	February 1996	Barany et al.	435/91.52

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY
130515	January 1985	EP
246864	November 1987	EP
0 320 308	June 1989	EP
324616	July 1989	EP
336731	October 1989	EP
89/09835	October 1989	WO

ART-UNIT: 189
PRIMARY-EXAMINER: Marschel; Ardin H.
ASSISTANT-EXAMINER: Riley; Jezia
ATTY-AGENT-FIRM: Nixon, Hagargrave, Devans & Doyle LLP

ABSTRACT:

The present invention relates to the cloning of the gene of a thermophilic DNA ligase, from Thermus aquaticus strain HB8, and the use of this ligase for the detection of specific sequences of nucleotides in a variety of nucleic acid samples, and more particularly in those samples containing a DNA sequence characterized by a difference in the nucleic acid sequence from a standard sequence including single nucleic acid base pair changes, deletions, insertions or translocations.
89 Claims, 9 Drawing figures

Main Menu | Search Form | Result Set | ShowS Numbers | Edit S Numbers | Referring Patents
First Hit | Previous Document | Next Document
Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC

Help | Logout

L3: 1 of 13

TITLE: Thermococcus barossii DNA polymerase mutants
US PAT NO: 5,882,904 [IMAGE AVAILABLE] DATE ISSUED: Mar. 16, 1999
APPL-NO: 08/906,925 DATE FILED: Aug. 4, 1997
US-CL-CURRENT: **435/91.2**, 194

SUMMARY:

BSUM(28)

In . . . in human DNA by amplifying a human target template gene sequence and exposing the sequence via APEX to a primer **array**. Upon successful hybridization and primer extension, the sequence of the template can be determined and potential mutations detected.

DETDESC:

DETD(8)

All . . . by automated sequence analysis for any manipulated region of the Tba DNA polymerase coding region. Restriction endonucleases and T4 DNA **ligase** were from either Pharmacia Biotech (Milwaukee, Wis.) or New England Biolabs (Beverly, Mass.). Taq DNA polymerase was from Perkin-Elmer (Perkin-Elmer. . .

2. 5,858,732, Jan. 12, 1999, Wide dynamic range nucleic acid detection using an aggregate primer series; Natalie A. Solomon, et al., **435/91.2**, 5, 6, 91.1; 536/24.3, 24.31, 24.33 [IMAGE AVAILABLE]

L3: 2 of 13

TITLE: Wide dynamic range nucleic acid detection using an aggregate primer series
US PAT NO: 5,858,732 [IMAGE AVAILABLE] DATE ISSUED: Jan. 12, 1999
APPL-NO: 08/697,404 DATE FILED: Aug. 23, 1996
REL-US-DATA: Continuation of Ser. No. 444,615, May 19, 1995, abandoned.
US-CL-CURRENT: **435/91.2**, 5, 6, 91.1; 536/24.3, 24.31, 24.33

SUMMARY:

BSUM(4)

Methods . . . Such methods include the polymerase chain reaction (PCR) which has been described in U.S. Pat. Nos. 4,683,195 and 4,683,202, the **ligase** chain reaction (LCR) described in EP-A-320 308, gap LCR (GLCR) described in European Patent Application EP-A-439 182, multiplex LCR described. . .

DETDESC:

DETD(18)

An . . . the target sequence are typically generated by the process of primer extension and/or ligation which utilizes enzymes with polymerase or **ligase** activity, separately or in combination, to add nucleotides to the hybridized primers and/or ligate adjacent primer pairs. While enzymatic methods. . .

DETDESC:

DETD(25)

According . . . As shown by FIG. 1, a strip of porous material 1 is spotted with capture reagents to form a diagonal **array** of capture spots 2.

DETDESC:

DETD(62)

The . . . EPPS buffer, pH 7.8; 20 mM K.sup.+ ; 30 mM MgCl.sub.2 ; 10 .mu.M NAD; 1.7 .mu.M TTP; 90 U/.mu.L **ligase** (Molecular Biology Resources; Milwaukee, Wis.), 0.01 U/.mu.L Taq polymerase (Perkin-Elmer; Norwalk, Conn.) and probes in concentrations shown in Table 5. . .

DETDESC:

DETD(66)

GLCR . . . jetted with 4 antibody spots (anti-adamantane, anti-quinoline, anti-dansyl and anti-fluorescein) from bottom left to upper right to form a diagonal **array** of capture spots. Each capture spot was jetted with 6.49.times.10.sup.-10 .mu.L of the antibody solutions. The anti-quinoline, anti-dansyl and anti-fluorescein. . .

3. 5,854,033, Dec. 29, 1998, Rolling circle replication reporter systems; Paul M. Lizardi, **435/91.2**, 6, 91.1; 536/23.1, 24.3 [IMAGE AVAILABLE]

L3: 3 of 13

TITLE: Rolling circle replication reporter systems
US PAT NO: 5,854,033 DATE ISSUED: Dec. 29, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/563,912 DATE FILED: Nov. 21, 1995
US-CL-CURRENT: **435/91.2**, 6, 91.1; 536/23.1, 24.3

SUMMARY:

BSUM(3)

A . . . acid detection. Most of these methods employ exponential amplification of targets or probes. These include the polymerase chain reaction (PCR), **ligase** chain reaction (LCR), self-sustained sequence replication (3SR), nucleic acid sequence based amplification (NASBA), strand displacement amplification (SDA), and amplification with. . .

DETDESC:

DETD(11)

An . . . has a 5' phosphate group and a 3' hydroxyl group. This allows the ends to be ligated using a DNA **ligase**, or extended in a gap-filling operation. Portions of the OCP have specific functions making the OCP useful for RCA and. . .

DETDESC:

DETD(57)

Solid-state . . . or supports to which address probes or detection molecules have been coupled. A preferred form of solid-state detector is an **array** detector. An **array** detector is a solid-state detector to which multiple different address probes or detection molecules have been coupled in an **array**, grid, or other organized pattern.

DETDESC:

DETD(71)

Any DNA **ligase** is suitable for use in the disclosed amplification method. Preferred ligases are those that preferentially form phosphodiester bonds at nicks. . . at a significant rate are preferred. Thermostable ligases are especially preferred. Many suitable ligases are known, such as T4 DNA **ligase** (Davis et al., Advanced Bacterial Genetics--A Manual for Genetic Engineering (Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1980)), E. coli DNA **ligase** (Panasnko et al., J. Biol. Chem. 253:4590-4592 (1978)), AMPLIGASE.RTM. (Kalin et al., Mutat. Res., 283(2):119-123 (1992); Winn-Deen et al., Mol Cell Probes (England) 7(3):179-186 (1993)), Taq DNA **ligase** (Barany, Proc. Natl. Acad. Sci. USA 88:189-193 (1991), Thermus thermophilus DNA **ligase** (Abbott Laboratories); Thermus scotoductus DNA **ligase** and Rhodothermus marinus DNA **ligase** (Thorbjarnardottir et al., Gene 151:177-180 (1995)). T4 DNA **ligase** is preferred for ligations involving RNA target sequences due to its ability to ligate DNA ends involved in DNA:RNA hybrids. . .

DETDESC:

DETD(72)

The frequency of non-target-directed ligation catalyzed by a **ligase** can be determined as follows. LM-RCA is performed with an open circle probe and a gap oligonucleotide in the presence. . .

DETDESC:

DETD(86)
(b) mixing **ligase** with the OCP-target sample mixture, resulting in a ligation mixture, and incubating the ligation mixture under conditions promoting ligation of. . .

DETDESC:

DETD(92)

An . . . types of ligases, those that are ATP-dependent and those that are NAD-dependent. ATP or NAD, depending on the type of **ligase**, should be present during ligation.

DETDESC:

DETD(93)

The **ligase** and ligation conditions can be optimized to limit the frequency of ligation of single-stranded termini. Such ligation events do not. . . molecules with single-stranded DNA termini will be ligated. This is based on the level of non-specific amplification seen with this **ligase** in the **ligase** chain reaction. Any higher nonspecific ligation frequency would cause enormously high background amplification in the **ligase** chain reaction. Using this estimate, an approximate frequency for the generation of non-specifically ligated open circles with a correctly placed. . .

DETDESC:

DETD(94)

When . . . such an operation is described in Example 4. Alternatively, an RNA target sequence can be detected directly by using a **ligase** that can perform ligation on a DNA:RNA hybrid substrate. A preferred **ligase** for this is T4 DNA **ligase**.

DETDESC:

DETD(105)

(c) Multiplexing and Hybridization **Array** Detection

DETDESC:

DETD(121)
(b) mixing **ligase** with the OCP-TS mixture, resulting in a secondary ligation mixture, and incubating the secondary ligation mixture under conditions promoting ligation. . .

DETDESC:

DETD(145)

Using a thermostable DNA **ligase**, such as AMPLIGASE.RTM. (Epicentre Technologies, Inc.), the open circle probe ligation reaction may be cycled a number of times between. . .

DETDESC:

DETD(146)

The expected net amplification yield using eight ligation cycles, secondary fluorescent tags, and **array** hybridization can be calculated as shown below.

DETDESC:

DETD(150)
20% **array** hybridization yield 0.2

DETDESC:

DETD(164)

A . . . have the same primer complement portion. Thus, both ligated open circle probes can be amplified using a single primer. Upon **array** hybridization, each detection probe would produce a unique signal, for

example, two alternative fluorescence colors, corresponding to the alternative target. . .

DETDESC:

DETD(168)
(a) The use of a thermostable DNA **ligase** such as AMPLIGASE.RTM. (Kalin et al. (1992)) or the T. thermophilus DNA **ligase** (Barany (1991)) will minimize the frequency of non-target-directed ligation events because ligation takes place at high temperature (50.degree. to 75.degree.. . .

DETDESC:

DETD(176)
(d) . . . target probe portions be designed with melting temperatures near suitable temperatures for the ligation operation. The use of a thermostable **ligase**, however, allows a wide range of ligation temperatures to be used, allowing greater freedom in the selection of target sequences.

DETDESC:

DETD(183)

Linear oligonucleotides with 5'-phosphates are efficiently ligated by **ligase** in the presence of a complementary target sequence. In particular, open circle probes hybridized to a target sequence as shown. . .

DETDESC:

DETD(185)
A . . . (pH 8.2), 25 mM KCl, 10 mM MgCl.sub.2, 0.5 mM NAD, 0.05% Triton X-100, in the presence of (a) DNA **ligase** (AMPLIGASE.RTM., Epicentre Technologies) at a concentration of 1 unit per 50 .mu.l, and (b) the following 5'-phosphorylated oligonucleotides:

DETDESC:

DETD(203)
T4 DNA **ligase** (New England Biolabs) is present at a concentration of 5 units per .mu.l, in a buffer consisting of 10 mM. . .

DETDESC:

DETD(212)

Each . . . dGTP, 1 Unit Thermus flavus DNA polymerase (lacking 3'-5' exonuclease activity; MBR, Milwaukee, Wis.), and 4000 Units Thermus thermophilus DNA **ligase** (Abbott laboratories). The reaction is incubated for 60 seconds at 85.degree. C., and 50 seconds at 60.degree. C. in a. . . if present, filling in of the gap space by the T. flavus DNA polymerase, and ligation by the T. thermophilus **ligase**. The discriminating nucleotide in the open circle probes above is the penultimate nucleotide. T. flavus DNA polymerase is used in the reaction to match the thermal stability of the T. thermophilus **ligase**.

DETDESC:

DETD(227)
T4 DNA **ligase** (New England Biolabs) is added at a concentration of 5 units per .mu.l, in a buffer consisting of 10 mM. . .

DETDESC:

DETD(238)

6. T4 DNA **ligase** (New England Biolabs) is added to each microtiter well at a concentration of 5 units per .mu.l, in a reaction. . .

CLAIMS:

CLMS(4)

4. . . .
under conditions that promote hybridization between the open circle probes and the target sequences in the OCP-target sample mixture,

(b) mixing **ligase** with the OCP-target sample mixture, to produce a ligation mixture, and incubating the ligation mixture under conditions that promote ligation. . .

CLAIMS:

CLMS(6)

6. . . .
probes and the target sequences and between the gap oligonucleotides and the target sequences in the OCP-target sample mixture,
(b) mixing **ligase** with the OCP-target sample mixture, to produce a ligation mixture, and incubating the ligation mixture under conditions that promote ligation. . .

4. 5,849,544, Dec. 15, 1998, Amplification and detection process; Raymond John Harris, et al., **435/91.2**, 6 [IMAGE AVAILABLE]

L3: 4 of 13

TITLE:	Amplification and detection process		
US PAT NO:	5,849,544 [IMAGE AVAILABLE]	DATE ISSUED:	Dec. 15, 1998
APPL-NO:	08/374,764	DATE FILED:	Jan. 24, 1995
FRN-PR. NO:	PL 3705	FRN FILED:	Jul. 24, 1992
FRN-PR. CO:	Australia		
PCT-NO:	PCT/AU93/00379	PCT-FILED:	Jul. 26, 1993
		371-DATE:	Jan. 24, 1995
		102(E)-DATE:	Jan. 24, 1995
PCT-PUB-NO:	WO94/02634	PCT-PUB-DATE:	Feb. 3, 1994
US-CL-CURRENT:	**435/91.2**, 6		

SUMMARY:

BSUM(3)

Various . . . number of recently developed in vitro nucleic acid amplification methods have greatly increased the sensitivity of detection. These methods include: **ligase** chain reaction (LCR), nucleic acid sequence based amplification (NASBA), Q.sub..beta. replicase based methods, strand displacement amplification (SDA) and notably polymerase. . .

DETDESC:

DETD(5)

The . . . cannot participate in polymerase mediated amplification. The 5'-end lacks a phosphate and, therefore, the capture probe cannot participate in LCR (**ligase** chain reaction).

DETDESC:

DETD(15)

Preferably, . . . complementary nucleic acid sequences. Thus, primer dimers--often formed during PCR--do not give false positives. For LCR, capture occurs across the **ligase** joined oligodeoxynucleotides.

DETDESC:

DETD(29)
(a) Microtitre trays composed of any plastic (e.g. polystyrene or polycarbonate), including tube assemblies (such as the 96 tube **array**) of Perkin Elmer Cetus for the GeneAmp PCR System 9000, standard 96 well (8.times.12) microtitre trays, such as Covalink trays. . .

DETDESC:

DETD(59)

This . . . from primer sequences and their complements. However, for methods where the amplified product is formed only from the primers (e.g. **Ligase** Chain Reaction, LCR), then the product target sequence will be in part of one strand of two joined primers and. . .

DETDESC:

DETD(110)
(a) . . . i.e. does not act as a primer for nucleic acid synthesis (e.g. for PCR) or does not act as a **ligase** substrate (e.g. for LCR).

DETDESC:

DETD(124)
(b) LCR (**Ligase** Chain Reaction)

DETDESC:

DETD(131)

See . . . genomic sequences and restriction site analysis for diagnosis of sickle cell anaemia", Science 230, pp 1350-1354, 1985. ##STR13## (b) LCR (**Ligase** Chain Reaction)

DETDESC:

DETD(132)

See F Barany, "Genetic disease detection and DNA amplification using cloned thermostable **ligase**", Proc Natl Acad Sci USA 88, pp 189-193, 1991. ##STR14## (c) NASBA (Nucleic Acid Sequence Based Amplification)

DETDESC:

DETD(146)
. . .
cycling

---

1. PCR + + + + + + +
2. LCR + + + + + Probably +

(**Ligase** chain reaction)
3. NASBA* + + + + + + No
RT/T7 42.degree. C. only
4. Q.beta. +. . .

CLAIMS:

CLMS(5)

5. The method of claim 4, wherein said amplification process is polymerase chain reaction; ligase chain reaction; nucleic acid sequence based amplification Q replicase dependent amplification or strand displacement amplification.

CLAIMS:

CLMS(19)

19. . . . 17, wherein the reagents for amplification of said target nucleic acid sequence are those for use in polymerase chain reaction, ligase chain reaction, nucleic acid sequence based amplification, Q replicase dependent amplification or strand displacement amplification.

5. 5,705,366, Jan. 6, 1998, Coamplification of target nucleic acids using volume exclusion agent in reaction composition, test kit and test device useful therefor; John W. Backus, 435/91.2, 5, 6; 536/23.1, 24.3, 24.32, 24.33 [IMAGE AVAILABLE]

L3: 5 of 13

TITLE: Coamplification of target nucleic acids using volume exclusion agent in reaction composition, test kit and test device useful therefor
US PAT NO: 5,705,366 DATE ISSUED: Jan. 6, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/306,792 DATE FILED: Sep. 15, 1994
US-CL-CURRENT: **435/91.2**, 5, 6; 536/23.1, 24.3, 24.32, 24.33

SUMMARY:

BSUM(6)

Much . . . greatly multiply the number of nucleic acids in a specimen for detection. Such amplification techniques include polymerase chain reaction (PCR), ligase chain reaction (LCR) and others which are less developed.

SUMMARY:

BSUM(15)

It . . . routinely added to reaction mixtures to "drive" unfavorable reactions forward. For example, they are added to reaction mixtures to "drive" ligase reactions, U.S. Pat. No. 5,185,243 (Ullman et al) and U.S. Pat. No. 5,194,370 (Berninger et al).

SUMMARY:

BSUM(96)
wherein . . . correlate very well with the values determined empirically at room temperature using conventional UV hypochromism and a conventional Hewlett-Packard diode array spectrophotometer (scanning rate of about +1.degree. C./min.) for a solution of primer in 10 mmolar tris(hydroxymethyl)aminomethane buffer (pH 8.5) having. . .

6. 5,654,179, Aug. 5, 1997, Nucleic acid preparation methods; Lily Lin, 435/91.2, 270; 436/177, 825; 536/25.4, 25.41, 25.42 [IMAGE AVAILABLE]

L3: 6 of 13

TITLE: Nucleic acid preparation methods
US PAT NO: 5,654,179 [IMAGE AVAILABLE] DATE ISSUED: Aug. 5, 1997
APPL-NO: 08/317,220 DATE FILED: Oct. 3, 1994
REL-US-DATA: Continuation of Ser. No. 44,649, Apr. 8, 1993, abandoned, which is a continuation-in-part of Ser. No. 901,545, Jun. 19, 1992, abandoned, which is a continuation-in-part of Ser. No. 614,921, Nov. 14, 1990, Pat. No. 5,284,940, Feb. 8, 1994.
US-CL-CURRENT: **435/91.2**, 270; 436/177, 825; 536/25.4, 25.41, 25.42

SUMMARY:

BSUM(6)

Where . . . been reported to inhibit virion-associated reverse transcriptase (RTase) of murine leukemia virus (MuLV) (Tsutsui and Mueller, BBRC 149:628-634, 1987), DNA **ligase** (Scher et al., Cancer Res. 48:6278-6284, 1988), cytoplasmic DNA polymerase (Byrnes et al., Biochem. 14:796-799, 1975), Taq polymerase (PCR Technology,. . .

SUMMARY:

BSUM(8)

Experiments with DNA ligase indicate that hemin at 4 .mu.M or less does not affect DNA ligase activity or DNA substrate integrity. Scher et al., supra. Pre-incubations of DNA ligase with hemin led to half-maximal inhibition of DNA ligase at hemin concentrations of 25-100 .mu.M (depending on the source of the DNA ligase). NAD-dependent DNA ligase from E. coli was not inhibited by hemin at concentrations up to 150 .mu.M. The inhibition of T4 DNA ligase activity and DNA ligase from mouse erythroleukemia (MEL) cells was not reversible by dilution, dialysis, or sucrose gradient centrifugation of cell-free extracts. Incubation of DNA ligase from MEL cells with hemoglobin was not inhibitory.

DETDESC:

DETD(5)

Template . . . a stringent specificity for its own promoters. M. Chamberlin et al., Nature 228:227 (1970). In the case of T4 DNA ligase, the enzyme will not ligate the two oligonucleotides where there is a mismatch between the oligonucleotide substrate and the template. . .

DETDESC:

DETD(22)

Where . . . major molecular forms, a 22,000 MW and an 11,000 MW form. Both forms have pronounced lytic activity on a vast array of bacteria.

7. 5,614,388, Mar. 25, 1997, PCR primers for detection of legionella species and methods for controlling visual intensity in hybridization assays; Teresa K.H. Picone, et al., 435/91.2, 6, 91.1, 822; 436/94; 536/23.1, 23.7, 24.32, 24.33, 25.3 [IMAGE AVAILABLE]

L3: 7 of 13

TITLE: PCR primers for detection of legionella species and methods for controlling visual intensity in hybridization assays

US PAT NO: 5,614,388 DATE ISSUED: Mar. 25, 1997
[IMAGE AVAILABLE]

APPL-NO: 08/455,116 DATE FILED: May 31, 1995

REL-US-DATA: Continuation of Ser. No. 70,328, May 27, 1993, Pat. No. 5,491,225, which is a continuation-in-part of Ser. No. 630,899, Dec. 20, 1990, abandoned.

US-CL-CURRENT: **435/91.2**, 6, 91.1, 822; 436/94; 536/23.1, 23.7, 24.32, 24.33, 25.3

SUMMARY:

BSUM(35)

"Amplification . . . multiplying the copies of a target sequence of nucleic acid. Such methods include but are not limited to PCR, DNA ligase, QB RNA replicase and RNA transcription-based amplification systems. These involve multiple amplification reagents and are more fully described below.

SUMMARY:

BSUM(107)

The . . . affixed to a solid support and PCR amplification product having biotin/streptavidin bound enzyme labels are used as detection probes. The array of capture probes on the solid support are three: (1) a first situs containing a mixture of 1:1 of the. . .

8. 5,612,201, Mar. 18, 1997, Isolated nucleic acid molecules useful in determining expression of a tumor rejection antigen precursor; Etienne De Plaen, et al., 435/91.2, 6; 536/23.1, 24.33 [IMAGE AVAILABLE]

L3: 8 of 13

TITLE: Isolated nucleic acid molecules useful in determining expression of a tumor rejection antigen precursor

US PAT NO: 5,612,201 DATE ISSUED: Mar. 18, 1997
[IMAGE AVAILABLE]

APPL-NO: 08/299,849 DATE FILED: Sep. 1, 1994

REL-US-DATA: Continuation-in-part of Ser. No. 37,230, Mar. 26, 1993, which is a continuation-in-part of Ser. No. 807,043, Dec. 12, 1991, Pat. No. 5,342,774, which is a continuation-in-part of Ser. No. 764,364, Sep. 23, 1991, Pat. No. 5,327,252, which is a continuation-in-part of Ser. No. 728,838, Jul. 9, 1991, abandoned, which is a continuation-in-part of Ser. No. 705,702, May 23, 1991, abandoned.

US-CL-CURRENT: **435/91.2**, 6; 536/23.1, 24.33

DETDESC:

DETD(133)

In . . . of the priming and hybridizing oligonucleotides. It can be concluded that the MAGE gene family is expressed by a large array of different tumors and that these genes are silent in the normal cells tested to this point.

DETDESC:

DETD(240)

Examples . . . an additional feature of the invention, as is their use in assays such as amplification assays (e.g., polymerase chain

reaction, ligase chain reaction), and so forth. They can also be used in standard hybridization assays, alone or in combinations. They can. . .

9. 5,565,339, Oct. 15, 1996, Compositions and methods for inhibiting dimerization of primers during storage of polymerase chain reaction reagents; Will Bloch, et al., 435/91.2; 422/102; 435/6 [IMAGE AVAILABLE]

L3: 9 of 13

TITLE: Compositions and methods for inhibiting dimerization of primers during storage of polymerase chain reaction reagents
US PAT NO: 5,565,339 [IMAGE AVAILABLE] DATE ISSUED: Oct. 15, 1996
APPL-NO: 08/325,134 DATE FILED: Oct. 20, 1994
REL-US-DATA: Continuation of Ser. No. 920,431, Oct. 8, 1992, abandoned.
US-CL-CURRENT: **435/91.2**; 422/102; 435/6

SUMMARY:

BSUM(84)

Water-in-grease . . . to phase-separate. Incorporation of a surfactant into either phase or both helps to stabilize the emulsion. Any of a large array of surfactants, preferably nonionic, are effective to this end, provided that they do not inhibit PCR and are used to. . .

SUMMARY:

BSUM(93)

Although . . . the transcription-based amplification system (Kwoh et al., 1989, Proc. Natl. Acad. Sci. USA 87:1874), amplification systems based on nucleic acid ligase (Wu and Wallace, 1989, Genomics 4:560, and Barringer et al., 1990, Gene 89:117), and amplification systems based on ribonuclease H. . .

10. 5,559,013, Sep. 24, 1996, Method of amplification using intermediate renaturation step; John W. Backus, et al., 435/91.2, 5, 6; 536/24.3, 24.33 [IMAGE AVAILABLE]

L3: 10 of 13

TITLE: Method of amplification using intermediate renaturation step
US PAT NO: 5,559,013 [IMAGE AVAILABLE] DATE ISSUED: Sep. 24, 1996
APPL-NO: 08/264,102 DATE FILED: Jun. 22, 1994
US-CL-CURRENT: **435/91.2**, 5, 6; 536/24.3, 24.33

SUMMARY:

BSUM(6)

Much . . . greatly multiple the number of nucleic acids in a specimen for detection. Such amplification techniques include polymerase chain reaction (PCR), ligase chain reaction (LCR) and others which are less developed.

SUMMARY:

BSUM(35)

Other amplification procedures which can be used in the practice of this invention include ligase chain reaction as described, for example, in EP-A-0 320 308 (published December, 1987) and EP-A-0 439 182 (published January, 1990),. . .

SUMMARY:

BSUM(64)
wherein . . . correlate very well with the values determined empirically at room temperature using conventional UV hypochromism and a conventional Hewlett-Packard diode array spectrophotometer (scanning rate of about +1.degree. C./min.) for a solution of primer in 10 mmolar tris(hydroxymethyl)aminomethane buffer (pH 8.5) having. . .

11. 5,427,932, Jun. 27, 1995, Repeat sequence chromosome specific

nucleic acid probes and methods of preparing and using; Heinz-Ulrich G. Weier, et al., 435/91.2, 6, 810; 436/501; 536/22.1, 23.1, 24.3, 24.31, 24.33 [IMAGE AVAILABLE]

L3: 11 of 13

TITLE: Repeat sequence chromosome specific nucleic acid probes and methods of preparing and using
US PAT NO: 5,427,932 DATE ISSUED: Jun. 27, 1995 [IMAGE AVAILABLE]
APPL-NO: 07/858,124 DATE FILED: Mar. 26, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 683,441, Apr. 9, 1991, abandoned.
US-CL-CURRENT: **435/91.2**, 6, 810; 436/501; 536/22.1, 23.1, 24.3, 24.31, 24.33

DETDESC:

DETD(135)

Newer techniques using the Q-beta replicase system [Lizardi et al. 1988] or ligase chain reaction, as commercialized by BioTechnica International Inc, [Cambridge Mass. (USA)], could be used to make copies of the desired. . .

DETDESC:

DETD(145)

In . . . in situ hybridization compared to the use of conventional clonal DNA probes, because it allows deposition of a very dense array of probes along the chromosomal target.

DETDESC:

DETD(203)

The . . . were then resuspended in 100 ul water. Two microliters of the DNA fragments were then resuspended in 30 ul 1.times. ligase buffer containing 10 units T4 DNA ligase and approximately 1 ug Bam HI-digested pBS DNA. The ligation was done at 15.degree. C. overnight. A 1 ul aliquot. . .

12. 5,278,051, Jan. 11, 1994, Construction of geometrical objects from polynucleotides; Nadrian C. Seeman, et al., 435/91.52, 91.3, 91.51; 536/23.1, 24.2 [IMAGE AVAILABLE]

L3: 12 of 13

TITLE: Construction of geometrical objects from polynucleotides
US PAT NO: 5,278,051 DATE ISSUED: Jan. 11, 1994 [IMAGE AVAILABLE]
APPL-NO: 07/805,564 DATE FILED: Dec. 12, 1991
US-CL-CURRENT: **435/91.52**, 91.3, 91.51; 536/23.1, 24.2

DETDESC:

DETD(22)

FIG. . . . left after BbvII cleavage, is added to the cleaved double-stranded first polynucleotide, the two become ligated when T4 or other ligase and cofactors such as ATP are added. The two strands of the formed segment have been designated as SEQ ID. . .

DETDESC:

DETD(84)

Ligations . . . mg/mL nuclease free bovine serum albumin (BRL), to which 66 .mu.M ATP has been added. 20-40 units of T4 polynucleotide ligase (U.S. Biochemical) are added, and the ligation proceeds at 16.degree.-22.degree. C. for 16-18 hours. The reaction is stopped by washing. . .

DETDESC:

DETD(96)

Solid-phase . . . 106, and then ligated (L) to give structure 132 with the two squares. Adding additional 102 and 104 widens the array.

Heat killing those that do not get through the last step ensures healthy growing lattices, and then restriction with enzyme. . .

DETDESC:

DETD(100)

Another . . . is added to the cleaved solid phase chain and their respective sticky ends are allowed to bind to each other. Ligase is added and the two molecules are ligated using the conditions in Example 1 to form new structure 170. Additional. . .

13. 4,888,286, Dec. 19, 1989, Production of gene and protein analogs through synthetic gene design using double stranded synthetic oligonucleotides; Roberto Crea, 435/91.52, 69.4, 91.53; 536/23.51 [IMAGE AVAILABLE]

L3: 13 of 13

TITLE: Production of gene and protein analogs through synthetic gene design using double stranded synthetic oligonucleotides

US PAT NO: 4,888,286 [IMAGE AVAILABLE] DATE ISSUED: Dec. 19, 1989

APPL-NO: 07/030,244 DATE FILED: Mar. 24, 1987

REL-US-DATA: Continuation of Ser. No. 577,130, Feb. 6, 1984, abandoned.

US-CL-CURRENT: **435/91.52**, 69.4, 91.53; 536/23.51

DRAWING DESC:

DRWD(8)

As . . . their self assembly through hydrogen bonding. Following this assembly, the structural gene is completed by enzymatic ligation using, e.g., DNA ligase. When required, single-stranded regions can be filled in with appropriate complementary bases using, e.g., DNA polymerase.

DRAWING DESC:

DRWD(17)

In . . . identify several amino acid doublets among those disclosed in Table 1. By assigning the appropriate codons, one can create an array of restriction endonuclease sites throughout a synthetic gene. In the case of hpGRF (see FIG. 1) several useful REN sites. . .

DETDESC:

DETD(10)

The . . . al., Biochemistry, 19:6096-6104 (1980). Generally, .sup.32 p-labeled oligomers were built into the hpGRF gene by a series of T.sub.4 DNA ligase - catalyzed reactions using the complementarity of overlapping fragments to insure proper ordering. Since fragment No. 1 and No. 22. . .

=> d 1-7

1. 5,879,884, Mar. 9, 1999, Diagnosis of depression by linkage of a polymorphic marker to a segment of chromosome 19P13 bordered by D19S247 and D19S394; Stephen J. Peroutka, 435/6, 5, 91.2; 536/24.3, 24.31, 24.32, 24.33 [IMAGE AVAILABLE]

2. 5,877,280, Mar. 2, 1999, Thermostable muts proteins; James G. Wetmur, 530/350; 435/6, 91.1; 436/94, 501 [IMAGE AVAILABLE]

3. 5,834,181, Nov. 10, 1998, High throughput screening method for sequences or genetic alterations in nucleic acids; Anthony P. Shuber, 435/5, 6, 91.1, 91.2 [IMAGE AVAILABLE]

4. 5,698,686, Dec. 16, 1997, Yeast telomerase compositions; Daniel E. Gottschling, et al., 536/23.1; 435/6, 91.2; 536/22.1, 24.3, 24.31, 24.33 [IMAGE AVAILABLE]

5. 5,578,450, Nov. 26, 1996, Tumor-specific genomic instability as a prognostic indicator; Steven N. Thibodeau, et al., 435/6, 91.2 [IMAGE AVAILABLE]

6. 5,449,604, Sep. 12, 1995, Chromosome 14 and familial Alzheimers disease genetic markers and assays; Gerard D. Schellenberg, et al., 435/6; 128/925; 435/91.2 [IMAGE AVAILABLE]

7. 5,403,708, Apr. 4, 1995, Methods and compositions for determining the sequence of nucleic acids; Thomas M. Brennan, et al., 435/6, 91.52; 436/94; 536/24.33, 25.32 [IMAGE AVAILABLE]

=> d 3 7 cit date hit

3. 5,834,181, Nov. 10, 1998, High throughput screening method for sequences or genetic alterations in nucleic acids; Anthony P. Shuber, 435/5, 6, 91.1, 91.2 [IMAGE AVAILABLE]

L5: 3 of 7

TITLE:	High throughput screening method for sequences or genetic alterations in nucleic acids		
US PAT NO:	5,834,181 [IMAGE AVAILABLE]	DATE ISSUED:	Nov. 10, 1998
APPL-NO:	08/710,134	DATE FILED:	Sep. 13, 1996
REL-US-DATA:	Continuation-in-part of Ser. No. 281,940, Jul. 28, 1994, Pat. No. 5,589,330, and a continuation-in-part of Ser. No. 485,885, Jun. 7, 1995.		

DETDESC:

DETD(12)

The present invention provides refinements of a modified allele-specific oligonucleotide approach for the simultaneous analysis of large numbers of patient samples for multiple CF mutations (25). Invention methods further provide a Multiplex Allele-Specific Diagnostic Assay (MASDA), which has the capacity to cost effectively analyze large numbers of samples (>500) for a large number of mutations (>100) in a single assay. Like the more familiar `chip` technologies (19-22), MASDA uses oligonucleotide hybridization to interrogate DNA sequences. However, in contrast to many oligonucleotide **array** approaches, in the invention MASDA technology, the target DNA is immobilized to the solid support, and interrogated in a combinatorial fashion with a pool of ASOs (i.e. a single mixture of mutation-specific oligonucleotides) in solution. By retaining the forward dot blot format, it is possible to simultaneously analyze large numbers of samples (>500) for a large number of mutations (>100). In phase I of the combinatorial analysis, the ASO(s) corresponding to the specific mutation(s) present in a given sample is hybrid-selected from the pool by the target DNA. Following removal of unhybridized ASOs, sequence-specific band patterns associated with the bound ASOs are generated by chemical or enzymatic sequencing, and the mutation or mutations present in the sample are easily identified. Using the gene targets CFTR (26), .beta.-globin (1), HEXA (27), GCR (28), ASPA (29), BRCA1 (3), and FACC (30) as a model system, we demonstrate that MASDA not only allows different patient samples with different disease

indications to be analyzed in a single assay, but allows the identification of multiple mutations within a single gene or multiple genes in a single patient's DNA sample.

DETDESC:

DETD(37)

Still further, hybridized polymers can be identified by use of hybridization arrays. In such arrays, purine and pyrimidine containing polymers of predetermined sequence are immobilized at discrete locations on a solid or semi-solid support. When used with the present invention, the sequence of each immobilized polymer comprising the **array** is complementary to the sequence of a member of the polymer pool. Members of the polymer pool that hybridize with target nucleic acids can be identified after separation from target nucleic acids by rehybridization with immobilized polymers forming the **array**. The identity of the polymer is determined by the location of hybridization on the **array**. See, U.S. Pat. No. 5,202,231 and WO 8910977.

DETDESC:

DETD(104)

For this protocol, the 96-well **array** of spotted genomic samples was marked with a grid so that positives identified in the hybridization could be easily located for the subsequent elution and ASO sequencing. Signal intensities generated from the different mutation-positive samples were optimized by adjusting the concentrations of each mutation-specific oligonucleotide within the hybridization. In order to achieve uniform hybridization signals, the final concentration of each labeled mutant ASO in the pool hybridization ranged from 0.008-1.8 pMol/ml, with the concentration of cold normal ASOs ranging from 0-200 fold excess of the corresponding mutant ASO.

DETDESC:

DETD(215)
14. Landegren, U., Kaiser, R., Sanders, J. and Hood, L. (1988) A **ligase-mediated** gene **detection** technique. Science, 241, 1077-1080.

7. 5,403,708, Apr. 4, 1995, Methods and compositions for determining the sequence of nucleic acids; Thomas M. Brennan, et al., 435/6, 91.52; 436/94; 536/24.33, 25.32 [IMAGE AVAILABLE]

L5: 7 of 7

TITLE:	Methods and compositions for determining the sequence of nucleic acids		
US PAT NO:	5,403,708 [IMAGE AVAILABLE]	DATE ISSUED:	Apr. 4, 1995
APPL-NO:	07/909,165	DATE FILED:	Jul. 6, 1992

SUMMARY:

BSUM(4)

The basic techniques for sequencing DNA include the Maxam-Gilbert chemical-degradation method (Maxam, A. M. and Gilbert, W. (1977) Proc. Natl. Acad. Sci. U.S.A. 74:560) and the dideoxy termination method of Sanger (Sanger, et al. (1977) Proc. Natl. Acad. Sci. U.S.A. 74:5463-5467). In addition, improvements have been made in conventional electrophoretic and capillary gel-based sequencing methods and various proposals have been made to use multiplexed vectors (Church, et al. (1988) Science 240:185), fluorescent single molecule exonuclease digestion (Keller, et al. (1989) J. Bio. Molecular Structure and Dynamics 7:301), scanning tunneling microscopy (Beebe, et al. (1989) Science 243:370), laser X-ray diffraction (Human Geno News 2, No. 2, paged 4 (1990)), laser deadsorption mass spectrometry (Williams, et al. (1989) Science 246:1585), sequencing by hybridization (Khrapko, et al. (1989) FEBS Letters 256:118; Bains, et al. (1988) J. Theoro. Biol. 135:303; and Drmanac, et al. (1988) Genomics 4:114), **array** determination of DNA sequence by mass spectrometry (U.S. Pat. No. 5,003,059), as well as suggestions to use isotopic sulfur (Brennan, et al., Biological Mass Spectrometry, page 159, Editor A. L. Burlingame, Elsevier (New York 1990)), or metals (Jacobson, et al. (1991) Anal. Chem. 63:402) and chemiluminescent detection systems (Bronstein, et al. (1990) BioTechniques 8:310). However, none of the foregoing methodologies

provide a comprehensive solution to the problem of large scale sequence analysis of genomes such as that of the human species.

DETDESC:

DETD(6)

When sequencing in the direction defined by one of the ends of the different ligation primers, generally the other end is blocked such that it cannot participate in a **ligase-mediated** reaction. For example, when a ligation product is being formed in a 5' to 3' direction (i.e., in the 3' to 5' direction on the single stranded nucleic acid template), the 5' end of the ligation primer is blocked, for example, by using a 5' dideoxy terminal nucleotide residue. When sequencing in the other direction, the terminal nucleotide residue of the ligation primer can be a 3' dideoxy nucleotide. Alternatively, the end of the ligation primer not participating in ligation product formation can be attached to one of the members of a binding pair to facilitate subsequent purification of the ligation product formed. Thus, the ligation primer can be attached to streptavidin or avidin or to an antigen or antibody or other member of a receptor-ligand binding pair. The other member of the binding pair can then be used to separate ligation product from other components of the reaction mixture, especially those components containing labeled nucleotide residues not incorporated into the ligation product, to facilitate subsequent **detection** of the labeled nucleotide residues incorporated into the ligation product.

=> d 1 kwic

US PAT NO: 5,879,884 [IMAGE AVAILABLE] L5: 1 of 7

DETDESC:

DETD(12)

"Variable . . . of tandem repeats" (VNTR's) are short sequences of nucleic acids arranged in a head to tail fashion in a tandem **array**, and found in each individual, as described in Wyman et al., Proc. Nat. Acad. Sci. 77:6754-6758 (1980). Generally, the VNTR. . .

DETDESC:

DETD(13)

"Dinucleotide . . . repeats are generally spread throughout the chromosomal DNA of an individual. The number of CA dinucleotides in any particular tandem **array** varies greatly from individual to individual, and thus, dinucleotide repeats may serve to generate restriction fragment length polymorphisms, and may. . .

DETDESC:

DETD(32)

The . . . is a homozygous variant (rare), only the variant probe binds. Paired probes for several variations can be immobilized as an **array** and the presence of several variations can thereby be analyzed simultaneously. Of course, the methods noted above, for analyzing uncharacterized. . .

DETDESC:

DETD(85)
6. **Ligase Mediated** Allele **Detection** Method

DETDESC:

DETD(86)

Target regions of a patients can be compared with target regions in unaffected and affected family members by **ligase-mediated** allele **detection**. See Landegren et al., Science 241:1077-1080 (1988). Ligase may also be used to detect point mutations in the ligation **amplification** reaction described in Wu et al., Genomics 4:560-569 (1989). The ligation **amplification** reaction (LAR) utilizes **amplification** of specific DNA sequence using sequential rounds of template dependent ligation as described in Wu, supra, and Barany, Proc.

Nat.. . .

=> d 1 date

L5: 1 of 7

TITLE: Diagnosis of depression by linkage of a polymorphic marker to a segment of chromosome 19P13 bordered by D19S247 and D19S394

US PAT NO: 5,879,884 DATE ISSUED: Mar. 9, 1999
[IMAGE AVAILABLE]

APPL-NO: 08/482,180 DATE FILED: Jun. 7, 1995

REL-US-DATA: Continuation-in-part of Ser. No. 366,288, Dec. 29, 1994, abandoned.